# DERIVATIVES OF SOME 2-ALKYLPIPERIDINES

By

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# PREFACE

The subject matter of this dissertation is divided into three sections. In the first section the syntheses of the intermediate 2-alkylpiperidines is presented. Reaction products of these piperidines with alkyl chlorocarbonates are presented in the second section. In the third section results of the reaction of the piperidines with bromomethyl ethyl sulfide are given. To facilitate the duplication or extension of this work, the material in each section is presented in detail.

The yields of the 2-alkylpiperidines are based upon the quantity of 2-picoline used in the synthesis.

Yields of carbamic acid esters and 1-ethylthiomethyl derivatives are based on the quantity of 2-alkylpiperidine used unless otherwise specified.

All temperatures refer to the centigrade scale, its symbol is omitted.

References are listed in the manner used by journals of the American Chemical Society. Abbreviations of journal names are those used by Chemical Abstracts.

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# CHAPTER I

## INTRODUCTION

In view of the physiological activity shown by some substituted carbamic acid esters prepared in this laboratory (30) it appeared advisable to extend the work in this field.

Since coniine (2-propylpiperidine), a naturally occurring alkaloid, exhibits marked physiological activity (6, 27) this seemed to be an appropriate starting material for the amine portion of the desired carbamic acid esters. From this it seemed a logical extension to substitute groups other than propyl on the two position of the piperidine ring.

On the basis of the foregoing facts and presumptions, it was decided to synthesize a series of 2-alkylpiperidines in which the alkyl group would vary from methyl through pentyl. Each of these substituted piperidines were then to be used in the preparation of a series of carbamic acid esters in which the alcohol fraction of the ester would be extended from methyl through hexyl using all commercially available alkyl chlorocarbonates which would yield products falling in this series.

In addition to the carbamic acid esters a series of compounds was prepared by reacting the 2-alkylpiperidines with bromomethyl ethyl sulfide. These compounds will be tested for physiological activity.

# CHAPTER II

# SYNTHESIS OF 2-ALKYLPIPERIDINES

## Review of Literature

The methods for the synthesis of specific 2-alkylpyridines and 2-alkylpiperidines were reviewed. All were rejected for use in this work except the reduction of 2-vinylpyridine to 2-ethylpiperidine (24). The rejections resulted from low yields reported, or unavailability of intermediates, and the fact that there were a number of methods reported which could be modified to general procedures for the preparation of any of the desired 2-alkylpiperidines.

The methods considered for use as general preparational procedures, fell into four catagories; reaction of pyridine with active metal-alkyls, cyclization reactions, reaction of 2-picoline with aldehydes, and reaction of picollyl alkali metal salts with alkyl halides.

The preparation of 2-pentylpiperidine reported by Franke and Prodinge (9) is a cyclization method. It involves the reaction of 1,5-dibromodecane with *p*-toluenesulfonamide to give the *p*-toluenesulfonamide of 2-pentylpiperidine. The unavailability of the appropriate 1,5-dihaloalkanes precluded this method from use as a general procedure. A similar situation arises in the method reported by Franke, Krupa and Schweitzer (14) by which they reacted 1-bromo-5-decanone with alcoholic ammonia in the preparation of 2-pentylpiperidine. The cyclization method reported by Salathiel, Burch and Hixon (17) is an entirely general one utilizing commercially available intermediates. It involves the reaction of the appropriate alkyl magnesium bromide with $\delta$ bromovaleronitrile and subsequent reduction to the alkyl piperidine. The cost of $\delta$ bromovaleronitrile in the quantities needed for this work would make this method very expensive.

The addition of Grignard reagents to pyridine, reported by Bergstrom and McAllister (8) has met with some controversy (22, 24, 26) and was not considered for use in this work for that reason. Ziegler and Zeiser (7) report the formation of 2-butylpyridine by the addition of butyllithium to pyridine. The one attempt at carrying out this reaction in this laboratory failed to yield the desired product.

The reaction of aldehydes with 2-picoline is probably one of the better general methods of obtaining 2-alkylpyridines. However, this method entails either dehydrating the alcohol formed (11) or replacing the hydroxyl group with a halide (4, 5) in order to reduce the chain to a saturated alkyl group.

The formation of alkali metal salts of 2-picoline and their reaction with alkyl halides to form 2-alkylpyridines has been widely used. Gregg and Craig (24) and

Prelog, Frenkiel and Szpilfogel (21) formed picolyl lithium and reacted it with the alkyl halides in the syntheses of 2-alkylpyridines containing one more carbon in the side chain than that contained in the chain of the alkyl halide. The same type of reaction has been carried out by a number of workers using picolyl sodium instead of picolyl lithium (16, 18, 29). This method does not encounter many of the difficulties or expenses which some of the above methods entail and was, therefore, the one chosen for this work.

Since sodium is somewhat easier to work with than lithium it was decided to use the sodium amide method of forming the alkali metal salt of 2-picoline. The precise method used is that given as "Method B" by Brown and Murphey (29).

Methods for the reduction of pyridine structures are of quite frequent occurrence in the literature. The only one considered suitable for the present work was the catalytic reduction using Raney nickel catalyst. The procedure used is essentially that of Adkins, Kuick and Wojcik (12, 13).

## Experimental Work

The same general method was used to prepare all the 2-alkylpiperidines above 2-methylpiperidine. 2-Ethylpiperidine was also prepared by the catalytic reduction of 2-vinylpyridine. Following are detailed directions for the preparation of 2-ethylpiperidine by the reduction of

2-vinylpyridine and by the general method by which 2-propyl, 2-butyl and 2-pentylpiperidines were also made. The preparation of 2-methylpiperidine involves only the catalytic reduction of 2-picoline and was carried out by the same method given for the reduction of 2-ethylpyridine.

Following the experimental directions are individual data sheets listing some of the properties of the 2-alkylpiperidines prepared.

## 2-Ethylpiperidine

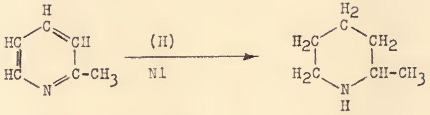
### (2-Propylpiperidine, 2-Butylpiperidine, 2-Pentylpiperidine)

Five hundred milliliters of liquid ammonia were placed in a one liter three-necked flask fitted with a mechanical stirrer. A catalytic amount (0.3 g.) of ferric nitrate hexahydrate was introduced and 28 g. (1.2 mole) of sodium was added in small pieces as the blue color from each successive addition disappeared. After the addition of sodium was completed the grey suspension was stirred for one hour. One mole (93.17 g.) of 2-picoline was introduced and the mixture was stirred for five to ten minutes. The solution became dark red on addition of the 2-picoline. Methyl bromide was added dropwise (1-1.5 hr.) until the red color just disappeared (one mole approx.). The mixture was stirred for one hour after the addition was completed and then allowed to stand until the ammonia evaporated. One hundred milliliters of water were added to the residue and the mixture was filtered. The organic layer was separated from the aqueous phase and the aqueous phase was washed with two 50 ml. portions of ether. The ether washings and the organic layer were combined and dried over sodium hydroxide flakes. The ether solution was decanted and fractionated at atmospheric pressure. Fifty-two grams of 2-ethylpyridine boiling at 148-151° were collected. The ethylpyridine and 5 g. of freshly prepared Raney nickel catalyst were placed in a rocking autoclave equipped with a hydrogenation spiral. Hydrogen was admitted to a pressure of two to four thousand pounds per square inch and the temperature was raised to 200°. After absorption of hydrogen ceased (4-6 hr.), the material was removed from the bomb, filtered and distilled. 2-Ethylpiperidine, boiling at 141-143°, was obtained in almost quantitative yield from the 2-ethylpyridine.

2-Propylpiperidine, 2-butylpiperidine and 2-pentylpiperidine were prepared by this same method, differing only in the use of ethyl bromide, propyl bromide and butyl chloride for the respective syntheses instead of methyl bromide.

## 2-Methylpiperidine

Equation for Synthesis:



| | |
|---|---|
| Molecular Formula | $C_6H_{13}N$ |
| Molecular Weight | 99.17 |
| Boiling Point | 117-118.5°/atm. |
| $N_D^{25}$ | 1.4463 |
| Yield of Product, % | 99 |

Solubility:

Soluble

Water

Ether

Alcohol

Benzene

## 2-Ethylpiperidine

### (By Reduction of 2-Vinylpyridine)

Commercial 2-vinylpyridine (250 g.) and 250 ml. of ethyl alcohol*, were placed in a 1000 ml. rocking autoclave with 10 g. of freshly prepared Raney nickel. Hydrogen was admitted, by means of a hydrogenation spiral, to a pressure of 2000 psi. The mixture was shaken for two hours at room temperature. The bomb was heated to 200° and maintained there until hydrogen absorption appeared to be complete. The material was removed from the bomb after it cooled and was subjected to a rough distillation through a Claisen head at atmospheric pressure. The fraction boiling from 125 to 175° was collected and fractionated through a distilling column rated at about ten plates. One hundred and five grams of 2-ethylpiperidine were collected, boiling at 141-143°/atm.

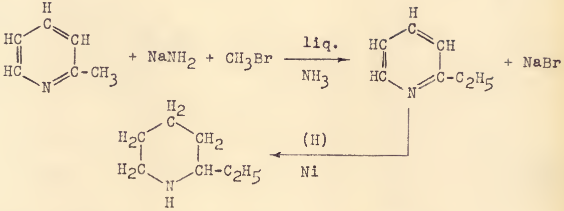
No yield was calculated as the 2-vinylpyridine used was partially polymerized. Calculation of a yield on the basis of figures given here would not give a true evaluation of the process.

---

*Due to partial polymerization, the 2-vinylpyridine was very viscous and would not have been mixed by the movement of the bomb if it had not been diluted. If freshly prepared 2-vinylpyridine is used, the solvent can be omitted.

## 2-Ethylpiperidine

Equation for Synthesis:



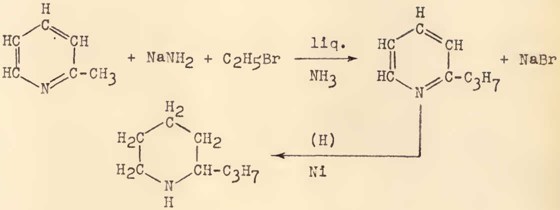
| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . | $C_7H_{15}N$ |
| Molecular Weight . . . . . . . . . . . . | 113.20 |
| Boiling Point . . . . . . . . . . . . . . | 141-143°/atm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . . . . . . | 1.4494 |
| Yield of Product, % . . . . . . . . . . . | 46 |

Solubility:

| Moderately Soluble | Soluble |
|---|---|
| Warm Water | Ether |
| | Alcohol |
| | Benzene |
| | Cold Water |

## 2-Propylpiperidine

Equation for Synthesis:



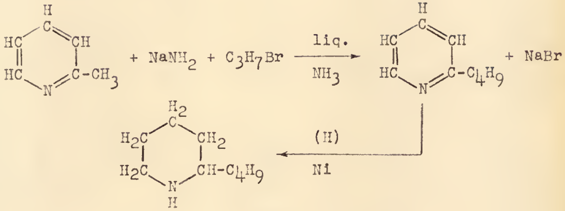
| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . | $C_8H_{17}N$ |
| Molecular Weight . . . . . . . . . . . . | 127.23 |
| Boiling Point . . . . . . . . . . . . . . | 167-168°/atm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . . . . | 1.4490 |
| Yield of Product, % . . . . . . . . . . . | 46.6 |

Solubility:

| Slightly Soluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

## 2-Butylpiperidine

Equation for Synthesis:



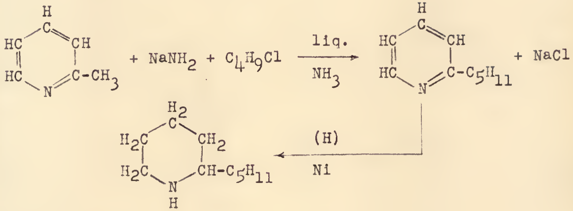
| | |
|---|---|
| Molecular Formula . . . . . . . . . . . | $C_9H_{19}N$ |
| Molecular Weight . . . . . . . . . . . | 141.25 |
| Boiling Point . . . . . . . . . . . . . | 98.8-99°/40 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . | 1.4508 |
| Yield of Product, % . . . . . . . . . . | 41.5 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

# 2-Pentylpiperidine

Equation for Synthesis:



| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . | $C_{10}H_{21}N$ |
| Molecular Weight . . . . . . . . . . . . | 155.28 |
| Boiling Point . . . . . . . . . . . . . . | 115.5-117°/40 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . | 1.4526 |
| Yield of Product, % . . . . . . . . . . . | 63.6 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

# CHAPTER III

# PRODUCTS FROM THE REACTION OF 2-ALKYLPIPERIDINES WITH ALKYL CHLOROCARBONATES

## Review of Literature

The reaction of amines with alkyl chlorocarbonates has been studied by a number of investigators (1, 2, 3, 10, 19, 28). The methods are all fundamentally the same, consisting of bringing the amine and chlorocarbonate together, with or without a diluting solvent, in the presence of an alkaline material to react with the hydrogen halide produced in the initial reaction.

## Experimental Work

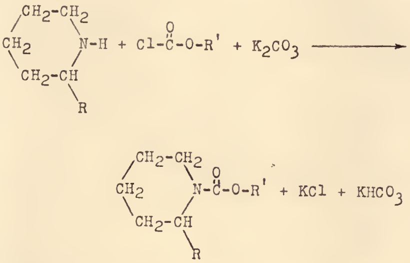
The best method for carrying out this reaction from a yield standpoint, would be to react the chlorocarbonate with a one mole excess of amine in an anhydrous, inert solvent such as ether or benzene. This would allow only the amine to be present as a possible reactant for the chlorocarbonate. The hydrogen chloride produced would be removed by the excess amine as insoluble amine hydrochloride. Use of this method is undesirable in that it entails the loss of considerable amounts of the amine or troublesome recovery of the amine from small batches of the amine hydrochloride.

The above procedure was used in one case in this work. In all the other preparations, in order to conserve the amines used, it was decided to use an inorganic substance to remove the hydrogen chloride produced. This was done by utilizing a two-phase reaction mixture; an aqueous solution of potassium carbonate and the 2-alkylpiperidine with or without a solvent, depending on its water solubility, as the nonaqueous phase.

Since chlorocarbonates are readily hydrolized by alkaline aqueous solutions, it is advisable to reduce its contact with such solutions. Since the chlorocarbonates are soluble in the nonaqueous phase, the arrangement given allows the chlorocarbonate being added, to contact and react with the amine in the nonaqueous phase, without undue contact with the aqueous phase. The amine hydrochloride formed from the hydrogen chloride produced dissolves in the aqueous phase where the amine is released by reaction with the alkali. The amine then separates from the aqueous phase or is extracted from it by the organic solvent. A solvent was used when 2-methyl, 2-ethyl and 2-propyl piperidines were reacted because of their water solubility. In the cases of 2-butyl and 2-pentylpiperidines a two phase system was formed between the piperidine and water solution without the use of an organic solvent.

Following are detailed directions for the work as it was done in this laboratory. Each preparation is followed by a data sheet listing some properties of the individual compounds prepared.

All of the preparations except that of 2-pentylpiperidine-1-carboxylic acid, methyl ester involve the following reaction scheme.



R represents the alkyl groups, methyl through pentyl and R' represents alkyl group, methyl through hexyl including 2-methyl propyl. The equation for the synthesis of 2-pentylpiperidine-1-carboxylic acid, methyl ester, is given on the data sheet for that compound.

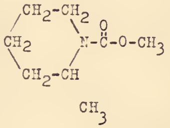
All the compounds presented in this chapter except 2-propylpiperidine-1-carboxylic acid, ethyl ester (2), are new to the literature.

## 2-Methylpiperidine-1-carboxylic Acid, Methyl Ester

In a Waring Blendor 200 g. of ice and 35 g. of potassium carbonate were stirred at high speed until the potassium carbonate was dissolved. Stirring was reduced to a slow rate by means of a variable transformer and a solution of 19.8 g. (0.20 mole) of 2-methypiperidine in 100 ml. of ether was introduced. With continued slow stirring 19.8 g. (0.21 mole) of methyl chlorocarbonate were added at a rapid drip rate. After the addition was completed the mixture was stirred until it warmed to about room temperature (1.5 hr. approx.). The ether layer was separated from the aqueous phase and dried over anhydrous potassium carbonate. The ether solution was filtered and low-boiling material was removed by use of water-pump vacuum and a steam bath. On distillation, the remaining oil yielded 16.1 g. (51.3%) of 2-methylpiperidine-1-carboxylic acid, methyl ester, boiling at 54-58°/1.0 mm.

## 2-Methylpiperidine-1-carboxylic Acid, Methyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . . | $C_8H_{15}NO_2$ |
| Molecular Weight . . . . . . . . . . . . | 157.21 |
| Boiling Point . . . . . . . . . . . . . . . | 54-58°/1.0 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . . | 1.4604 |
| Yield of Product, % . . . . . . . . . . . | 51.3 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

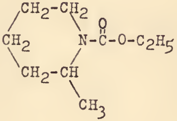
| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 61.12 | .... | 60.89 |
| Hydrogen, % . | 9.62 | .... | 9.94 |

## 2-Methylpiperidine-1-carboxylic Acid, Ethyl Ester

In a 500 ml. three-necked flask, fitted with mechanical stirrer and dropping funnel, were placed solutions of 50 g. of potassium carbonate in 100 ml. of water and 24.79 g. (0.25 mole) of 2-methylpiperidine in 200 ml. of ether. The mixture was stirred at room temperature and 27.1 g. (0.25 mole) of ethyl chlorocarbonate was added dropwise (30 min.). After the addition was completed, the ether layer was separated from the aqueous phase and dried over anhydrous sodium sulfate. The solution was decanted and volatile material was removed by means of water-pump vacuum and a steam bath. On distillation, the remaining oil yielded 25.5 g. (59.6%) of 2-methylpiperidine-1-carboxylic acid, ethyl ester, boiling at 67.5°/1.0 mm.

## 2-Methylpiperidine-1-carboxylic Acid, Ethyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula | $C_9H_{17}NO_2$ |
| Molecular Weight | 171.24 |
| Boiling Point | 67.5°/1.0 mm. |
| $N_D^{25}$ | 1.4558 |
| Yield of Product, % | 60 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

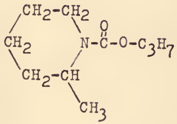
| | Calculated | Found |
|---|---|---|
| Carbon, % | 63.12 | 63.52 |
| Hydrogen, % | 9.95 | 10.14 |

## 2-Methylpiperidine-1-carboxylic Acid, Propyl Ester

In a 500 ml. three-necked flask fitted with mechanical stirrer and dropping funnel were placed solutions of 50 g. of potassium carbonate in 100 ml. of water and 19.83 g. (0.20 mole) of 2-methylpiperidine in 200 ml. of ether. The mixture was cooled in an ice bath and stirred during addition (10 min.) of 24.5 g. (0.20 mole) of propyl chlorocarbonate. After the addition was completed the mixture was stirred thirty minutes without cooling. The ether layer was separated from the aqueous phase and low-boiling material was evaporated on the steam bath. The remaining oil was dried over anhydrous sodium sulfate. On filtration and distillation, the oil yielded 20.2 g. (54.5%) of 2-methylpiperidine-1-carboxylic acid, propyl ester, boiling at 69-70°/1.0 mm.

## 2-Methylpiperidine-1-carboxylic Acid, Propyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . . | $C_{10}H_{19}NO_2$ |
| Molecular Weight . . . . . . . . . . . . . | 185.26 |
| Boiling Point . . . . . . . . . . . . . . . | 69-70°/1.0 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . . . . | 1.4559 |
| Yield of Product, % . . . . . . . . . . . | 54.5 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

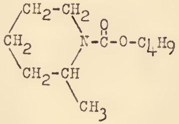
| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 64.83 | .... | 64.95 |
| Hydrogen, % . | 10.34 | .... | 10.59 |

## 2-Methylpiperidine-1-carboxylic Acid, Butyl Ester

In a 500 ml. three-necked flask fitted with mechanical stirrer and dropping funnel were placed solutions of 25 g. of potassium carbonate in 100 ml. of water and 19.8 g. (0.20 mole) of 2-methylpiperidine in 200 ml. of ether. The mixture was cooled in an ice bath and stirred during the addition (10-15 min.) of 35.0 g. (0.257 mole) of butyl chlorocarbonate. The mixture was stirred without cooling for fifteen minutes after the addition was completed. Twenty-five grams of potassium carbonate was then added and stirring continued thirty minutes without cooling. The ether layer was separated from the aqueous phase and low-boiling material was removed by use of water-pump vacuum and a steam bath. On distillation, the remaining oil yielded 30.2 g. (76.2%) of 2-methylpiperidine-1-carboxylic acid, butyl ester, boiling at 80-82°/1.0 mm.

## 2-Methylpiperidine-1-carboxylic Acid, Butyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . . | $C_{11}H_{21}NO_2$ |
| Molecular Weight . . . . . . . . . . . . . | 199.29 |
| Boiling Point . . . . . . . . . . . . . . . | 82°/1.0 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . . | 1.4563 |
| Yield of Product, % . . . . . . . . . . . | 76.2 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

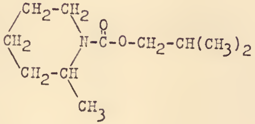
| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 66.29 | .... | 65.97 |
| Hydrogen, % . | 10.62 | .... | 10.55 |

### 2-Methylpiperidine-1-carboxylic Acid, 2-Methylpropyl Ester

In a 500 ml. three-necked flask fitted with mechanical stirrer and dropping funnel were placed solutions of 19.8 g. (0.20 mole) of 2-methylpiperidine in 100 ml. of ether and 35 g. of potassium carbonate in 200 ml. of water. The mixture was cooled in an ice bath and stirred during the addition (1 hr.) of 34 g. (0.25 mole) of 2-methylpropyl chlorocarbonate. After the addition was completed five grams of potassium carbonate were added and stirring continued for one hour without cooling. The ether layer was separated from the aqueous phase and dried over anhydrous calcium sulfate. The ether solution was decanted and low-boiling material was removed by use of water-pump vacuum and a steam bath. On distillation the remaining oil yielded 32.5 g. (81.5%) of 2-methylpiperidine-1-carboxylic acid, 2-methylpropyl ester, boiling at 73.5-76°/1.0 mm.

## 2-Methylpiperidine-1-carboxylic Acid, 2-Methylpropyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . | $C_{11}H_{21}NO_2$ |
| Molecular Weight . . . . . . . . . . . . | 199.29 |
| Boiling Point . . . . . . . . . . . . . . | 76°/1.0 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . . | 1.4539 |
| Yield of Product, % . . . . . . . . . . . | 81.5 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

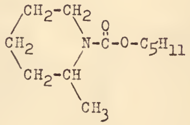
| Analyses: | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 66.29 | .... | 66.15 |
| Hydrogen, % . | 10.62 | .... | 10.75 |

## 2-Methylpiperidine-1-carboxylic Acid, Pentyl Ester

In a 500 ml. three-necked flask fitted with mechanical stirrer and dropping funnel were placed solutions of 40 g. of potassium carbonate in 100 ml. of water and 19.9 g. (0.20 mole) of 2-methylpiperidine in 200 ml. of ether. The mixture was cooled in an ice bath and stirred during the addition (30 min.) of 25.5 g. (0.22 mole) of pentyl chlorocarbonate. After the addition was completed the mixture was stirred for thirty minutes without cooling. The ether layer was separated from the aqueous phase and dried over anhydrous calcium sulfate. The ether solution was filtered and low-boiling material was removed by means of water-pump vacuum and a steam bath. On distillation, the remaining oil yielded 30.1 g. (70.6%) of 2-methylpiperidine-1-carboxylic acid, pentyl ester. A crystalline solid precipitated from the product and was removed by several 10 ml. water washes. Qualitative tests indicated the solid material to be 2-methylpiperidine hydrochloride. Redistillation of the oil gave a boiling point of 92°/1.0 mm. and no appreciable residue.

# 2-Methylpiperidine-1-carboxylic Acid, Pentyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . | $C_{12}H_{23}NO_2$ |
| Molecular Weight . . . . . . . . . . . . | 213.31 |
| Boiling Point . . . . . . . . . . . . . | 92°/1.0 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . . . | 1.4571 |
| Yield of Product, % . . . . . . . . . . . | 83.4 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

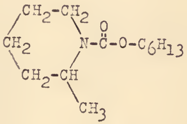
| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 67.56 | .... | 67.45 |
| Hydrogen, % . | 10.87 | .... | 10.75 |

## 2-Methylpiperidine-1-carboxylic Acid, Hexyl Ester

In a 500 ml. three-necked flask fitted with mechanical stirrer and dropping funnel were placed solutions of 40 g. of potassium carbonate in 100 ml. of water and 19.8 g. (0.20 mole) of 2-methylpiperidine in 200 ml. of ether. The mixture was cooled in an ice bath and stirred during addition (20 min.) of 27 g. (0.20 mole) of hexyl chlorocarbonate. After the addition was completed the mixture was stirred ten minutes without cooling. The ether layer was separated from the aqueous phase and dried over anhydrous calcium sulfate. The ether solution was filtered and low-boiling material was removed by use of water-pump vacuum and a steam bath. On distillation, the remaining oil yielded 31.4 g. (68.1%) of 2-methylpiperidine-1-carboxylic acid, hexyl ester, boiling at 103°/1.0 mm. White crystals precipitated from the product and were removed by several water washes. Qualitative tests indicated the solid to be 2-methylpiperidine hydrochloride. Redistillation of the oil gave a boiling point of 103°/1 mm. and no appreciable residue.

## 2-Methylpiperidine-1-carboxylic Acid, Hexyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . . | $C_{13}H_{25}NO_2$ |
| Molecular Weight . . . . . . . . . . . . . | 227.34 |
| Boiling Point . . . . . . . . . . . . . . . | 103°/1.0 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . . . | 1.4579 |
| Yield of Product, % . . . . . . . . . . . | 84.3 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

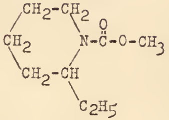
| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 68.68 | .... | 68.55 |
| Hydrogen, % . | 11.08 | .... | 10.95 |

## 2-Ethylpiperidine-1-carboxylic Acid, Methyl Ester

In a Waring Blendor 200 g. of ice and 40 g. of potassium carbonate were stirred at high speed until the potassium carbonate was dissolved. Stirring was reduced to a slow rate by means of a variable transformer and a solution of 22.6 g. (0.20 mole) of 2-ethylpiperidine in 200 ml. of ether was introduced. With continued slow stirring, 18.9 g. (0.20 mole) of methyl chlorocarbonate were added dropwise (30 min.). The mixture was stirred for one hour after the addition was completed. The ether solution was separated from the aqueous phase and dried over anhydrous potassium carbonate. The ether solution was decanted and low-boiling material was removed by means of water-pump vacuum and a steam bath. On distillation the remaining oil yielded 19.5 g. (57%) of 2-ethylpiperidine-1-carboxylic acid, methyl ester, boiling at 62-64°/1.0 mm.

## 2-Ethylpiperidine-1-carboxylic Acid, Methyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . . | $C_9H_{17}NO_2$ |
| Molecular Weight . . . . . . . . . . . . | 171.24 |
| Boiling Point . . . . . . . . . . . . . . | 62-64°/1.0 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . . . | 1.4960 |
| Yield of Product, % . . . . . . . . . . . | 57 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

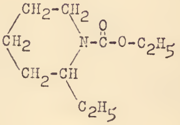
| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 63.12 | .... | 62.80 |
| Hydrogen, % . | 10.01 | .... | 9.83 |

## 2-Ethylpiperidine-1-carboxylic Acid, Ethyl Ester

In a Waring Blendor 200 g. of ice and 40 g. of potassium carbonate were stirred at high speed until the potassium carbonate was dissolved. Stirring was reduced to a slow rate by means of a variable transformer and a solution of 22.6 g. (0.20 mole) of 2-ethylpiperidine in 200 ml. of ether was introduced. With continued slow stirring 21.7 g. (0.20 mole) of ethyl chlorocarbonate were added dropwise (30 min.). The mixture was stirred for one hour after the addition was completed. The ether solution was separated from the aqueous phase and dried over anhydrous potassium carbonate. The solution was decanted and low-boiling material was removed by means of water-pump vacuum and a steam bath. On distillation, the remaining oil yielded 23.8 g. (64.2%) of 2-ethylpiperidine-1-carboxylic acid, ethyl ester, boiling at 68.5-70°/1.0 mm.

## 2-Ethylpiperidine-1-carboxylic Acid, Ethyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . | $C_{10}H_{19}NO_2$ |
| Molecular Weight . . . . . . . . . . . . | 185.26 |
| Boiling Point . . . . . . . . . . . . . . | 68.5-70°/1.0 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . . | 1.4560 |
| Yield of Product, % . . . . . . . . . . . | 64.2 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

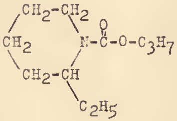
| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 64.83 | .... | 64.65 |
| Hydrogen, % . | 10.34 | .... | 10.54 |

## 2-Ethylpiperidine-1-carboxylic Acid, Propyl Ester

In a Waring Blendor, 200 g. of ice and 40 g. of potassium carbonate were stirred at high speed until the potassium carbonate was dissolved. Stirring was reduced to a slow rate by means of a variable transformer and a solution of 22.6 g. (0.20 mole) of 2-ethylpiperidine in 200 ml. of ether was introduced. With continued slow stirring, 24.5 g. (0.20 mole) of propyl chlorocarbonate were added dropwise (30 min.). The mixture was stirred for one hour after the addition was completed. The ether solution was separated from the aqueous phase and dried over anhydrous potassium carbonate. The solution was decanted and low-boiling material was removed by means of water-pump vacuum and a steam bath. On distillation, the remaining oil yielded 28.6 g. (71.8%) of 2-ethylpiperidine-1-carboxylic acid, propyl ester, boiling at 80-81°/1.0 mm.

## 2-Ethylpiperidine-1-carboxylic Acid, Propyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula | $C_{11}H_{21}NO_2$ |
| Molecular Weight | 199.29 |
| Boiling Point | 80-81°/1.0 mm. |
| $N_D^{25}$ | 1.4559 |
| Yield of Product, % | 71.8 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

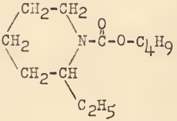
| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 66.29 | .... | 66.02 |
| Hydrogen, % . | 10.62 | .... | 10.80 |

## 2-Ethylpiperidine-1-carboxylic Acid, Butyl Ester

In a Waring Blendor, 200 g. of ice and 40 g. of potassium carbonate were stirred at high speed until the potassium carbonate was dissolved. Stirring was reduced to a slow rate by means of a variable transformer and a solution of 22.6 g. (0.20 mole) of 2-ethylpiperidine in 200 ml. of ether was introduced. With continued slow stirring, half of 27.3 g. (0.20 mole) of butyl chlorocarbonate was added immediately and the remainder was added dropwise (30 min.). The mixture was stirred for fifteen minutes after the addition was completed. The ether solution was separated from the aqueous phase and dried over anhydrous potassium carbonate. The solution was decanted and low-boiling material was removed by means of water-pump vacuum and a steam bath. On distillation, the remaining oil yielded 33.6 g. (78.9%) of 2-ethylpiperidine-1-carboxylic acid, butyl ester, boiling at 91.5-92°/1.0 mm.

## 2-Ethylpiperidine-1-carboxylic Acid, Butyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula | $C_{12}H_{23}NO_2$ |
| Molecular Weight | 213.31 |
| Boiling Point | 91.5-92°/1.0 mm. |
| $N_D^{25}$ | 1.4567 |
| Yield of Product, % | 78.9 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

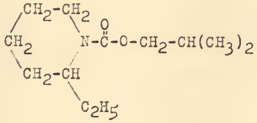
| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 67.56 | .... | 66.93 |
| Hydrogen, % . | 10.87 | .... | 11.19 |

### 2-Ethylpiperidine-1-carboxylic Acid, 2-Methylpropyl Ester

In a Waring Blendor 200 g. of ice and 40 g. of potassium carbonate were stirred at high speed until the potassium carbonate was dissolved. Stirring was reduced to a slow rate by means of a variable transformer and a solution of 22.6 g. (0.20 mole) of 2-ethylpiperidine in 200 ml. of ether was introduced. With continued slow stirring, half of 27.3 g. (0.20 mole) of 2-methylpropyl chlorocarbonate was added immediately and the remainder was added dropwise (15 min.). The mixture was stirred for thirty minutes after the addition was completed. The ether solution was separated from the aqueous phase and dried over anhydrous potassium carbonate. The solution was decanted and low-boiling material was removed by means of water-pump vacuum and a steam bath. On distillation, the remaining oil yielded 36.4 g. (87.4%) of 2-ethylpiperidine-1-carboxylic acid, 2-methylpropyl ester, boiling at 87-89°/1.0 mm.

## 2-Ethylpiperidine-1-carboxylic Acid, 2-Methylpropyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . . | $C_{12}H_{23}NO_2$ |
| Molecular Weight . . . . . . . . . . . . . | 213.31 |
| Boiling Point . . . . . . . . . . . . . . | 87-89°/1.0 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . . | 1.4538 |
| Yield of Product, % . . . . . . . . . . . | 87.4 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

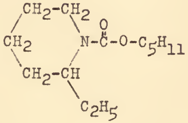
| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 67.56 | .... | 68.44 |
| Hydrogen, % . | 10.87 | .... | 10.69 |

## 2-Ethylpiperidine-1-carboxylic Acid, Pentyl Ester

In a Waring Blendor 200 g. of ice and 40 g. of potassium carbonate were stirred at high speed until the potassium carbonate was dissolved. Stirring was reduced to a slow rate and a solution of 17 g. (0.15 mole) of 2-ethylpiperidine in 200 ml. of ether was introduced. With continued slow stirring, half of 23 g. (0.15 mole) of pentyl chlorocarbonate was added immediately and the remainder was added dropwise (60 min.). The mixture was stirred for two hours after the addition was completed. The ether solution was separated from the aqueous phase and dried over anhydrous potassium carbonate. The solution was decanted and low-boiling material was removed by means of water-pump vacuum and a steam bath. On distillation the remaining oil yielded 24.5 g. (72%) of 2-ethylpiperidine-1-carboxylic acid, pentyl ester, boiling at 104-106°/1.0 mm.

## 2-Ethylpiperidine-1-carboxylic Acid, Pentyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . | $C_{13}H_{25}NO_2$ |
| Molecular Weight . . . . . . . . . . . | 227.34 |
| Boiling Point . . . . . . . . . . . . . | 104-106°/1.0 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . | 1.4570 |
| Yield of Product, % . . . . . . . . . . | 72 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

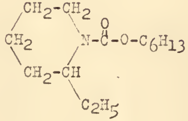
| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 68.68 | .... | 68.85 |
| Hydrogen, % . | 11.08 | .... | 11.26 |

## 2-Ethylpiperidine-1-carboxylic Acid, Hexyl Ester

A mixture of 100 g. of ice, 100 ml. of water and 35 g. of potassium carbonate was placed in an 800 ml. beaker and stirred with a magnetic stirrer until the potassium carbonate was dissolved. Stirring was reduced to a moderate rate and a solution of 17 g. (0.15 mole) of 2-ethylpiperidine in 200 ml. of ether was introduced. With continued moderate stirring, half of 24.8 g. (0.15 mole) of hexyl chlorocarbonate was added immediately and the remainder was added dropwise (30 min.). The mixture was stirred for ninety minutes after the addition was completed. The ether layer was separated from the aqueous phase and dried over anhydrous potassium carbonate. The ether solution was decanted and low-boiling material was removed by means of water-pump vacuum and a steam bath. On distillation, the remaining oil yielded 25.5 g. (70.3%) of 2-ethylpiperidine-1-carboxylic acid, hexyl ester, boiling at 115.5-117.5°/1.0 mm.

## 2-Ethylpiperidine-1-carboxylic Acid,
## Hexyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . | $C_{14}H_{27}NO_2$ |
| Molecular Weight . . . . . . . . . . . | 241.37 |
| Boiling Point . . . . . . . . . . . . . | 115.5-117.5°/1.0 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . | 1.4546 |
| Yield of Product, % . . . . . . . . . . | 70.3 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

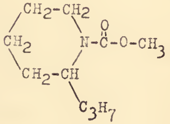
| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 69.66 | .... | 69.03 |
| Hydrogen, % . | 11.28 | .... | 11.33 |

## 2-Propylpiperidine-1-carboxylic Acid, Methyl Ester

In a 500 ml. three-necked flask fitted with mechanical stirrer and dropping funnel, were placed solutions of 31.8 g. (.025 mole) of 2-propylpiperidine in 200 ml. of ether and 50 g. of potassium carbonate in 100 ml. of water. The mixture was cooled in an ice bath and stirred during addition (2.5 hrs.) of 27.2 g. (0.288 mole) of methyl chlorocarbonate. The mixture was stirred about one hour after the addition was completed. The ether layer was separated from the aqueous phase and dried over anhydrous sodium sulfate. The solution was decanted and low-boiling material was removed by use of water-pump vacuum and a steam bath. On distillation, the remaining oil yielded 33.9 g. (73.2%) of 2-propylpiperidine-1-carboxylic acid, methyl ester, boiling at 68°/1.0 mm.

## 2-Propylpiperidine-1-carboxylic Acid, Methyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . . | $C_{10}H_{19}NO_2$ |
| Molecular Weight . . . . . . . . . . . . . | 185.25 |
| Boiling Point . . . . . . . . . . . . . . | 68°/1.0 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . . | 1.4604 |
| Yield of Product, % . . . . . . . . . . . | 73.2 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

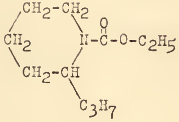
| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 64.83 | .... | 64.78 |
| Hydrogen, % . | 10.34 | .... | 10.35 |

## 2-Propylpiperidine-1-carboxylic Acid, Ethyl Ester

In a 500 ml. three-necked flask, fitted with mechanical stirrer and dropping funnel, were placed solutions of 50 g. of potassium carbonate in 100 ml. of water and 36.5 g. (0.286 mole) of 2-propylpiperidine in 200 ml. of ether. The mixture was cooled in an ice bath during the addition (2.5 hr.) of 31 g. (0.285 mole) of ethyl chlorocarbonate. After the addition was completed the ether layer was separated from the aqueous phase and dried over anhydrous sodium sulfate. The ether solution was decanted and low-boiling material was removed by use of water-pump vacuum and a steam bath. On distillation, the remaining oil yielded 23 g. (40.5%) of 2-propylpiperidine-1-carboxylic acid, ethyl ester, boiling at 65-67°/1.0 mm.

## 2-Propylpiperidine-1-carboxylic Acid, Ethyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . . | $C_{11}H_{21}NO_2$ |
| Molecular Weight . . . . . . . . . . . . | 199.28 |
| Boiling Point . . . . . . . . . . . . . . | 87°/2.2 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . . . | 1.4570 |
| Yield of Product, % . . . . . . . . . . . | 40.5 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

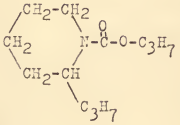
| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 66.29 | .... | 65.99 |
| Hydrogen, % . | 10.62 | .... | 10.52 |

## 2-Propylpiperidine-1-carboxylic Acid, Propyl Ester

In a 500 ml. three-necked flask fitted with mechanical stirrer and dropping funnel, were placed solutions of 50 g. of potassium carbonate in 100 ml. of water and 31.8 g. (0.25 mole) of 2-propylpiperidine in 200 ml. of ether. The mixture was cooled in an ice bath and stirred during addition of half of 30.7 g. (0.25 mole) of propyl chlorocarbonate. The mixture was then stirred six hours while warming to room temperature. The mixture was again cooled and the remainder of the chlorocarbonate was added dropwise (30 min.). The ether layer was separated from the aqueous phase and dried over anhydrous sodium sulfate. The ether solution was decanted and low-boiling material was removed by means of water-pump vacuum and a steam bath. On distillation, the remaining oil yielded 46.2 g. (86.7%) of 2-propylpiperidine-1-carboxylic acid, propyl ester, boiling at 89°/1.0 mm.

## 2-Propylpiperidine-1-carboxylic Acid, Propyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . . | $C_{12}H_{23}NO_2$ |
| Molecular Weight . . . . . . . . . . . . . | 213.31 |
| Boiling Point . . . . . . . . . . . . . . | 86°/1.0 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . . . | 1.4570 |
| Yield of Product, % . . . . . . . . . . . | 86.7 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

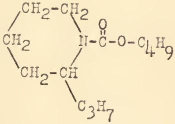
| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 67.56 | .... | 67.62 |
| Hydrogen, % . | 10.87 | .... | 10.72 |

## 2-Propylpiperidine-1-carboxylic Acid, Butyl Ester

In a 500 ml. three-necked flask fitted with mechanical stirrer and dropping funnel, were placed solutions of 31.8 g. (0.25 mole) of 2-propylpiperidine in 200 ml. of ether and 50 g. of potassium carbonate in 100 ml. of water. The mixture was cooled in an ice bath and stirred during the addition (1.5-2 hrs.) of 34.14 g. (0.25 mole) of butyl chlorocarbonate. The mixture was stirred for fifteen minutes after the addition was completed. The ether layer was separated from the aqueous phase and dried over anhydrous sodium sulfate. The solution was decanted and low-boiling material was removed by use of water-pump vacuum and a steam bath. The remaining oil was distilled but a crystalline solid precipitated from the distillate. Qualitative tests indicated the solid to be 2-propylpiperidine hydrochloride. The distillate was washed several times with water and dried over anhydrous potassium carbonate. On redistillation, the oil yielded 42.5 g. (74%) of 2-propylpiperidine-1-carboxylic acid, butyl ester, boiling at 96-100°/1.0 mm.

## 2-Propylpiperidine-1-carboxylic Acid, Butyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . . | $C_{13}H_{25}NO_2$ |
| Molecular Weight . . . . . . . . . . . . . | 227.34 |
| Boiling Point . . . . . . . . . . . . . . | 90.5-91.5°/1.0 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . . | 1.4549 |
| Yield of Product, % . . . . . . . . . . . | 74 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

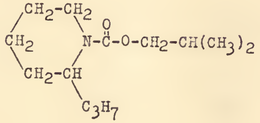
| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 68.68 | .... | 68.95 |
| Hydrogen, % . | 11.08 | .... | 11.21 |

## 2-Propylpiperidine-1-carboxylic Acid, 2-Methylpropyl Ester

In a 500 ml. three-necked flask fitted with mechanical stirrer and dropping funnel were placed solutions of 40 g. of potassium carbonate in 100 ml. of water and 25.4 g. (0.20 mole) of 2-propylpiperidine in 200 ml. of ether. The mixture was cooled in an ice bath and stirred during addition (70 min.) of 30 g. (0.22 mole) of 2-methylpropyl chlorocarbonate. Stirring was continued for thirty minutes without cooling after the addition was completed. The ether layer was separated from the aqueous phase and dried over anhydrous calcium sulfate. The ether solution was decanted and low-boiling material was removed by use of water-pump vacuum and a steam bath. On distillation, the remaining oil yielded 27.6 g. (60.7%) of 2-propylpiperidine-1-carboxylic acid, 2-methylpropyl ester, boiling at 93.5-94°/1.0 mm.

# 2-Propylpiperidine-1-carboxylic Acid, 2-Methylpropyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula . . . . . . . . . . . | $C_{13}H_{25}NO_2$ |
| Molecular Weight . . . . . . . . . . . | 227.38 |
| Boiling Point . . . . . . . . . . . . . | 93-94°/1.0 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . | 1.4560 |
| Yield of Product, % . . . . . . . . . . . | 60.7 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

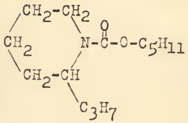
| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 68.68 | .... | 68.47 |
| Hydrogen, % . | 11.08 | .... | 10.98 |

## 2-Propylpiperidine-1-carboxylic Acid, Pentyl Ester

In a 500 ml. three-necked flask, fitted with mechanical stirrer and dropping funnel, were placed solutions of 40 g. of potassium carbonate in 100 ml. of water and 25.4 g. (0.20 mole) of 2-propylpiperidine in 200 ml. of ether. The mixture was cooled in an ice bath and stirred during the addition (130 min.) of 25.5 g. (0.169 mole) of pentyl chlorocarbonate. The mixture was stirred without cooling for one hour after the addition was completed. The ether layer was separated from the aqueous phase and dried over anhydrous calcium sulfate. The ether solution was decanted, and low-boiling material was removed by use of water-pump vacuum and a steam bath. Distillation of the remaining oil gave a water-white product. Crystalline solid precipitated from the product. Qualitative tests indicated the solid to be 2-propylpiperidine hydrochloride. The product was redissolved in 100 ml. of ether and washed with 50 ml. of 25% potassium carbonate solution. Evaporation of the ether and distillation of the oil yielded 29 g. (71% based upon the pentyl chlorocarbonate) of 2-propylpiperidine-1-carboxylic acid, pentyl ester, boiling at 105°/1.0 mm.

## 2-Propylpiperidine-1-carboxylic Acid,
## Pentyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . | $C_{14}H_{27}NO_2$ |
| Molecular Weight . . . . . . . . . . . | 241.37 |
| Boiling Point . . . . . . . . . . . . . | 105-107°/1.0 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . | 1.4578 |
| Yield of Product, % . . . . . . . . . . | 71 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

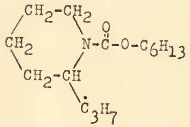
| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 69.66 | .... | 70.40 |
| Hydrogen, % . | 11.28 | .... | 11.38 |

## 2-Propylpiperidine-1-carboxylic Acid, Hexyl Ester

In a 500 ml. three-necked flask fitted with mechanical stirrer and dropping funnel were placed solutions of 40 g. of potassium carbonate in 100 ml. of water and 25.4 g. (0.20 mole) of 2-propylpiperidine in 200 ml. of ether. The mixture was cooled in an ice bath and stirred during the addition (75 min.) of 27 g. (0.16 mole) of hexyl chlorocarbonate. The mixture was stirred for thirty minutes without cooling after the addition was completed. The ether layer was separated from the aqueous phase and dried over anhydrous calcium sulfate. The ether solution was decanted and low-boiling material was removed by use of water-pump vacuum and a steam bath. Distillation of the remaining oil gave a yellow liquid from which a crystalline solid precipitated. Qualitative tests indicated the solid to be 2-propylpiperidine hydrochloride. The product was redissolved in 100 ml. of ether and washed with 50 ml. of 25% potassium carbonate solution. Evaporation of the ether and distillation of the oil yielded 31 g. (73% based upon the hexyl chlorocarbonate) 2-propylpiperidine-1-carboxylic acid, hexyl ester, boiling at 119-120°/1.0 mm.

## 2-Propylpiperidine-1-carboxylic Acid, Hexyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . . | $C_{15}H_{29}NO_2$ |
| Molecular Weight . . . . . . . . . . . . | 255.39 |
| Boiling Point . . . . . . . . . . . . . . | 119-120°/1.0 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . . . | 1.4583 |
| Yield of Product, % . . . . . . . . . . . | 73.6 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

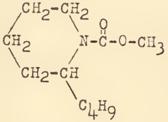
| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 70.54 | .... | 70.89 |
| Hydrogen, % . | 11.45 | .... | 11.63 |

## 2-Butylpiperidine-1-carboxylic Acid, Methyl Ester

In a Waring Blendor 200 g. of ice and 40 g. of potassium carbonate were stirred at high speed until the potassium carbonate was dissolved. Stirring was reduced to a slow rate by means of a variable transformer, and 34.3 g. (0.24 mole) of 2-butylpiperidine were introduced. With continued slow stirring, 20 g. (0.201 mole) of methyl chlorocarbonate were added dropwise, (10-15 min.). The mixture was stirred until it warmed to about room temperature (90 min.). The oil which formed was separated from the aqueous phase and washed twice with 5 ml. portions of 0.1$\underline{N}$ silver nitrate— 1.0$\underline{N}$ nitric acid solution. Both of these washes were basic on separation from the oil. The oil was returned to the blendor with 200 g. of ice and 20 g. of potassium carbonate and treated with an additional 5 g. of methyl chlorocarbonate. The oil was separated from the aqueous phase and washed with 10 ml. of the silver nitrate-nitric acid solution. After drying over anhydrous calcium sulfate the oil was distilled, yielding 26.1 g. (54%) of 2-butylpiperidine-1-carboxylic acid, methyl ester, boiling at 84-86°/1.0 mm.

## 2-Butylpiperidine-1-carboxylic Acid, Methyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . . | $C_{11}H_{21}NO_2$ |
| Molecular Weight . . . . . . . . . . . . | 199.29 |
| Boiling Point . . . . . . . . . . . . . . | 84-86°/1.0 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . . . | 1.4610 |
| Yield of Product, % . . . . . . . . . . . | 65 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

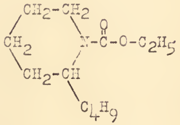
| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 66.29 | .... | 66.25 |
| Hydrogen, % . | 10.62 | .... | 10.71 |

## 2-Butylpiperidine-1-carboxylic Acid, Ethyl Ester

In a Waring Blendor 200 g. of ice and 40 g. of potassium carbonate were stirred at high speed until the potassium carbonate was dissolved. Stirring was reduced to a slow rate by means of a variable transformer and 34.3 g. (0.244 mole) of 2-butylpiperidine were introduced. With continued slow stirring, 22 g. (0.202 mole) of ethyl chlorocarbonate were added slowly (10-15 min.). The mixture was stirred for eighty minutes after the addition was completed. The organic layer was separated from the aqueous phase, washed with 6 ml. of 1N nitric acid— 0.1N silver nitrate solution, filtered and dried over anhydrous calcium sulfate. On distillation, the remaining oil yielded 32 g. (74% based upon the ethyl chlorocarbonate) of 2-butylpiperidine-1-carboxylic acid, ethyl ester, boiling at 90.5-92°/1.0 mm.

## 2-Butylpiperidine-1-carboxylic Acid, Ethyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . | $C_{12}H_{23}NO_2$ |
| Molecular Weight . . . . . . . . . . . . | 213.31 |
| Boiling Point . . . . . . . . . . . . . . | 90.5-92°/1.0 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . | 1.4573 |
| Yield of Product, % . . . . . . . . . . | 74 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

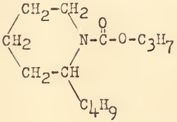
| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 67.56 | .... | 67.54 |
| Hydrogen, % . | 10.87 | .... | 10.91 |

## 2-Butylpiperidine-1-carboxylic Acid, Propyl Ester

In a Waring Blendor 200 g. of ice and 40 g. of potassium carbonate were stirred at high speed until the potassium carbonate was dissolved. Stirring was reduced to a slow rate by means of a variable transformer and 21.9 g. (0.15 mole) of 2-butylpiperidine were introduced. With continued slow stirring 18.5 g. (0.15 mole) of propyl chlorocarbonate were added dropwise (15-20 min.). The mixture was stirred for one hour after the addition was completed. The organic layer was separated from the aqueous phase and washed with 15 ml. of 1$\underline{N}$ nitric acid—0.1$\underline{N}$ silver nitrate solution. On distillation, the remaining oil yielded 13.4 g. (40.7%) of 2-butylpiperidine-1-carboxylic acid, propyl ester, boiling at 100°/1.0 mm.

## 2-Butylpiperidine-1-carboxylic Acid, Propyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . . | $C_{13}H_{25}NO_2$ |
| Molecular Weight . . . . . . . . . . . . . | 227.34 |
| Boiling Point . . . . . . . . . . . . . . | 100°/1.0 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . . . | 1.4588 |
| Yield of Product, % . . . . . . . . . . . | 40.7 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

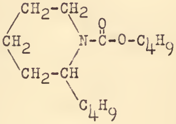
| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 68.68 | .... | 68.81 |
| Hydrogen, % . | 11.08 | .... | 11.35 |

### 2-Butylpiperidine-1-carboxylic Acid, Butyl Ester

In a Waring Blendor 200 g. of ice and 40 g. of potassium carbonate were stirred at high speed until the potassium carbonate was dissolved. Stirring was reduced to a slow rate by means of a variable transformer and 21.19 g. (0.15 mole) of 2-butylpiperidine were introduced. With contined slow stirring, 20.6 g. (0.15 mole) of butyl chlorocarbonate were added slowly (15-20 min). The mixture was stirred for one hour after the addition was completed. The organic layer was separated from the aqueous phase, washed with 10 ml. of 1N nitric acid– 0.1N silver nitrate solution, centrifuged to remove solid matter and dried over anhydrous calcium sulfate. On distillation, the remaining oil yielded 21 g. (66%) of 2-butylpiperidine-1-carboxylic acid, butyl ester, boiling at 110.5°/1.0 mm.

## 2-Butylpiperidine-1-carboxylic Acid, Butyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula | $C_{14}H_{27}NO_2$ |
| Molecular Weight | 241.37 |
| Boiling Point | 110.5°/1.0 mm. |
| $N_D^{25}$ | 1.4580 |
| Yield of Product, % | 66 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

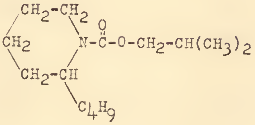
| | Calculated | Found |
|---|---|---|
| Carbon, % | 69.66 | 69.63 |
| Hydrogen, % | 11.28 | 11.37 |

## 2-Butylpiperidine-1-carboxylic Acid, 2-Methylpropyl Ester

In a Waring Blendor 200 g. of ice and 25 g. of potassium carbonate were stirred at high speed until the potassium carbonate was dissolved. Stirring was reduced to a slow rate by means of a variable transformer and 21.19 g. (0.15 mole) of 2-butylpiperidine were introduced. With continued slow stirring 20.6 g. (0.15 mole) of 2-methylpropyl chlorocarbonate were added slowly (10-15 min.). The organic layer was separated from the aqueous phase, washed with 10 ml. of 1*N* nitric acid-0.1*N* silver nitrate solution, centrifuged to remove solid matter and dried over anhydrous calcium sulfate. On distillation the remaining oil yielded 27.7 g. (78%) of 2-butylpiperidine-1-carboxylic acid, 2-methylpropyl ester, boiling at 108-109°/1.0 mm.

## 2-Butylpiperidine-1-carboxylic Acid, 2-Methylpropyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . | $C_{14}H_{27}NO_2$ |
| Molecular Weight . . . . . . . . . . . . | 241.37 |
| Boiling Point . . . . . . . . . . . . . . | 108-109°/1.0 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . . | 1.4561 |
| Yield of Product, % . . . . . . . . . . | 78 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

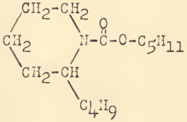
| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 69.66 | .... | 69.54 |
| Hydrogen, % . | 11.28 | .... | 11.30 |

## 2-Butylpiperidine-1-carboxylic Acid, Pentyl Ester

In a Waring Blendor 200 g. of ice and 25 g. of potassium carbonate were stirred at high speed until the potassium carbonate was dissolved. Stirring was reduced to a slow rate by means of a variable transformer and 21.19 g. (0.15 mole) of 2-butylpiperidine were introduced. With continued slow stirring 22.7 g. (0.15 mole) of pentyl chlorocarbonate were added slowly (10-15 min.). The mixture was stirred for one hour after the addition was completed. The organic layer which formed was separated from the aqueous phase, washed with 10 ml. of 1N nitric acid-0.1N silver nitrate solution, centrifuged to remove solid matter and dried over anhydrous calcium sulfate. On distillation the remaining oil yielded 31.8 g. (81%) of 2-butylpiperidine-1-carboxylic acid, pentyl ester, boiling at 121-122°/1.0 mm.

## 2-Butylpiperidine-1-carboxylic Acid, Pentyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . | $C_{15}H_{29}NO_2$ |
| Molecular Weight . . . . . . . . . . . . | 255.39 |
| Boiling Point . . . . . . . . . . . . . . | 121-122°/1.0 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . | 1.4581 |
| Yield of Product, % . . . . . . . . . . | 81 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

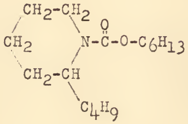
| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 70.54 | .... | 70.79 |
| Hydrogen, % . | 11.45 | .... | 11.27 |

## 2-Butylpiperidine-1-carboxylic Acid, Hexyl Ester

In a Waring Blendor, 200 g. of ice and 25 g. of potassium carbonate were stirred at high speed until the potassium carbonate was dissolved. Stirring was reduced to a slow rate by means of a variable transformer and 21.19 g. (0.15 mole) of 2-butylpiperidine were introduced. With continued slow stirring, 25 g. (0.15 mole) of hexyl chlorocarbonate were added slowly (10-15 min.). The mixture was stirred for one hour after the addition was completed. The organic layer which formed was separated from the aqueous phase and dried over anhydrous calcium sulfate. A crystalline solid precipitated from the material after it was distilled. Qualitative tests indicated the solid to be 2-butylpiperidine hydrochloride. The product was washed with potassium carbonate solution (25%) and redistilled. Twenty-four grams (59.5%) of 2-butylpiperidine-1-carboxylic acid, hexyl ester were obtained, boiling at 134-135°/1.0 mm.

## 2-Butylpiperidine-1-carboxylic Acid, Hexyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula | $C_{16}H_{31}NO_2$ |
| Molecular Weight | 269.42 |
| Boiling Point | 134-135°/1.0 mm. |
| $N_D^{25}$ | 1.4578 |
| Yield of Product, % | 59.5 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

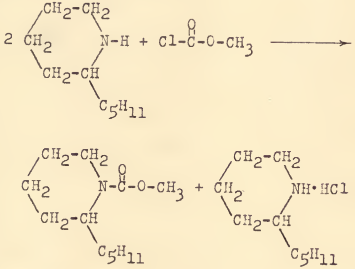
| | Calculated | Found |
|---|---|---|
| Carbon, % | 71.32 | 71.32 |
| Hydrogen, % | 11.60 | 11.90 |

## 2-Pentylpiperidine-1-carboxylic Acid, Methyl Ester

Two tenths of a mole (31.06 g.) of 2-pentylpiperidine was placed in a 250 ml. Erlenmeyer flask and methyl chlorocarbonate was added until no further reaction was noted. Considerable heat was generated, and material was lost due to vaporization. 2-Pentylpiperidine hydrochloride precipitated. Fifty milliliters of water were added, dissolving the salt. The mixture was cooled in an ice bath and potassium carbonate was added until the aqueous layer was basic to litmus. An oil precipitated and was separated from the aqueous phase. Distillation of the oil yielded 25 g. (58.5%) of 2-pentylpiperidine-1-carboxylic acid, methyl ester, boiling at 91.5°/1.0 mm.

## 2-Pentylpiperidine-1-carboxylic Acid, Methyl Ester

Equation for Synthesis:



| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . . | $C_{12}H_{23}NO_2$ |
| Molecular Weight . . . . . . . . . . . . | 213.31 |
| Boiling Point . . . . . . . . . . . . . | 91.5°/1.0 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . . | 1.4609 |
| Yield of Product, % . . . . . . . . . . . | 58.5 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

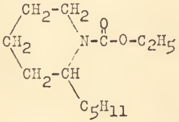
| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 67.56 | .... | 67.55 |
| Hydrogen, % . | 10.87 | .... | 11.05 |

## 2-Pentylpiperidine-1-carboxylic Acid, Ethyl Ester

One hundred grams of ice and 40 g. of potassium carbonate were placed in a Waring Blendor and stirred at high speed until the potassium carbonate was dissolved. Stirring was reduced to a slow rate by means of a variable transformer, and 31 g. (0.20 mole) of 2-pentylpiperidine were introduced into the blendor. With continued slow stirring, 21.7 g. (0.20 mole) of ethyl chlorocarbonate were added dropwise (10 min.). Slow stirring was continued until the mixture warmed to about room temperature (about 90 min.). The oil which formed was separated from the aqueous phase and dried over anhydrous calcium sulfate. The oil was filtered and distilled, yielding 35.3 g. (78%) of yellow liquid. A small amount of crystalline solid precipitated from the product. Qualitative tests indicated the solid to be 2-pentylpiperidine hydrochloride. The product was washed with 5 ml. of 0.1$\underline{N}$ silver nitrate-1$\underline{N}$ nitric acid solution. On redistillation of the oil, 2-pentylpiperidine-1-carboxylic acid, ethyl ester was obtained as a yellow liquid boiling at 100-103°/1.0 mm.

## 2-Pentylpiperidine-1-carboxylic Acid, Ethyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . . | $C_{13}H_{25}NO_2$ |
| Molecular Weight . . . . . . . . . . . . | 227.34 |
| Boiling Point . . . . . . . . . . . . . . . | 100-103°/1.0 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . . . | 1.4579 |
| Yield of Product, % . . . . . . . . . . . | 78 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

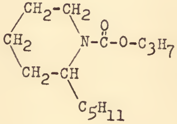
| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 68.68 | .... | 68.48 |
| Hydrogen, % . | 11.08 | .... | 11.12 |

## 2-Pentylpiperidine-1-carboxylic Acid, Propyl Ester

In a Waring Blendor 200 g. of ice and 40 g. of potassium carbonate were stirred at high speed until the potassium carbonate was dissolved. Stirring was reduced to a slow rate by means of a variable transformer, and 31.1 g. (0.20 mole) of 2-pentylpiperidine were introduced. With continued slow stirring 24.5 g. (0.20 mole) of propyl chlorocarbonate were added dropwise (10-15 min.). The mixture was stirred until it warmed to about room temperature (90 min.). The oil which formed was separated from the aqueous layer and dried over anhydrous calcium sulfate. The oil was filtered and distilled, yielding 36.5 g. (75.5%) of 2-pentylpiperidine-1-carboxylic acid, propyl ester, boiling at 112-113°/1.0 mm. A small amount of crystalline solid precipitated from the product. Qualitative tests indicate the solid to be 2-pentylpiperidine hydrochloride. The product was washed with 5 ml. of 0.1N silver nitrate-1.0N nitric acid solution. Redistillation of the oil gave no change in the boiling point and practically no residue.

## 2-Pentylpiperidine-1-carboxylic Acid, Propyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula | $C_{14}H_{27}NO_2$ |
| Molecular Weight | 241.37 |
| Boiling Point | 112-113°/1.0 mm. |
| $N_D^{25}$ | 1.4580 |
| Yield of Product, % | 75.2 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

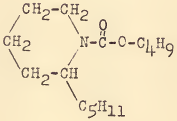
| | Calculated | Found |
|---|---|---|
| Carbon, % | 69.66 | 69.65 |
| Hydrogen, % | 11.28 | 11.16 |

## 2-Pentylpiperidine-1-carboxylic Acid, Butyl Ester

In a Waring Blendor 200 g. of ice and 40 g. of potassium carbonate were stirred at high speed until the potassium carbonate was dissolved. Stirring was reduced to a slow rate by means of a variable transformer, and 31.1 g. (0.20 mole) of 2-pentylpiperidine were introduced. With continued slow stirring, 27.5 g. (0.20 mole) of butyl chlorocarbonate were added dropwise (15-20 min.). The mixture was stirred until it warmed to about room temperature (90 min.). The oil which formed was separated from the aqueous phase and dried over anhydrous calcium sulfate. The material was filtered and distilled, yielding 38 gm. (74.5%) of 2-pentylpiperidine-1-carboxylic acid, butyl ester, boiling at 122-124°/1.0 mm.

## 2-Pentylpiperidine-1-carboxylic Acid,
## Butyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula | $C_{15}H_{29}NO_2$ |
| Molecular Weight | 255.39 |
| Boiling Point | 122-124°/1.0 mm. |
| $N_D^{25}$ | 1.4586 |
| Yield of Product, % | 74.5 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

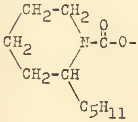
| | Calculated | Found |
|---|---|---|
| Carbon, % | 70.54 | 70.67 |
| Hydrogen, % | 11.45 | 11.62 |

## 2-Pentylpiperidine-1-carboxylic Acid,
## 2-Methylpropyl Ester

In a Waring Blendor 200 g. of ice and 40 g. of potassium carbonate were stirred at high speed until the potassium carbonate was dissolved. Stirring was then reduced to a slow rate by means of a variable transformer, and 31.1 g. (0.20 mole) of 2-pentylpiperidine were introduced. With continued slow stirring, 27.5 g. (0.201 mole) of 2-methylpropyl chlorocarbonate were added dropwise (10 to 15 min.). The mixture was then stirred until it warmed to about room temperature (90 min.). The oil which formed was separated from the aqueous phase and dried over anhydrous calcium sulfate. The material was filtered and distilled, yielding 43.2 g. (76%) of 2-pentylpiperidine-1-carboxylic acid, 2-methylpropyl ester, boiling at 120-122°/1.0 mm.

### 2-Pentylpiperidine-1-carboxylic Acid, 2-Methylpropyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . | $C_{15}H_{29}NO_2$ |
| Molecular Weight . . . . . . . . . . . | 255.39 |
| Boiling Point . . . . . . . . . . . . . . | 120-122°/1.0 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . . . | 1.4564 |
| Yield of Product, % . . . . . . . . . . . | 76.2 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

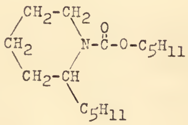
| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 70.54 | .... | 70.43 |
| Hydrogen, % . | 11.45 | .... | 11.55 |

## 2-Pentylpiperidine-1-carboxylic Acid, Pentyl Ester

In a Waring Blendor 200 g. of ice and 40 g. of potassium carbonate were stirred at high speed until the potassium carbonate was dissolved. Stirring was reduced to a slow rate by means of a variable transformer and 31.1 g. (0.20 mole) of 2-pentylpiperidine were introduced. With continued slow stirring 30.3 g. (0.20 mole) of amyl chlorocarbonate were added dropwise (15-20 min.). The mixture was stirred for fifteen minutes after the addition was completed. The organic layer was separated from the aqueous phase and dried over anhydrous calcium sulfate. The oil was decanted and distilled. Crystalline solid precipitated from the product. Qualitative tests indicated the solid to be 2-pentylpiperidine hydrochloride. The product was washed with 10 ml. of 0.1N silver nitrate-1N nitric acid solution. On redistillation, the oil yielded 12 g. (23%) of 2-pentylpiperidine-1-carboxylic acid, pentyl ester, boiling at 134°/1.0 mm.

## 2-Pentylpiperidine-1-carboxylic Acid, Pentyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . | $C_{16}H_{31}NO_2$ |
| Molecular Weight . . . . . . . . . . . . | 269.42 |
| Boiling Point . . . . . . . . . . . . . . | 134°/1.0 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . . . | 1.4587 |
| Yield of Product, % . . . . . . . . . . . | 23 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

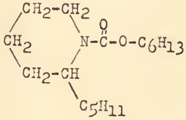
| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 71.32 | .... | 71.14 |
| Hydrogen, % . | 11.60 | .... | 11.36 |

## 2-Pentylpiperidine-1-carboxylic Acid, Hexyl Ester

In a Waring Blendor 200 g. of ice and 40 g. of potassium carbonate were stirred at high speed until the potassium carbonate was dissolved. Stirring was reduced to a slow rate by means of a variable transformer, and 31.1 g. (0.20 mole) of 2-pentylpiperidine were introduced. With continued slow stirring, 33 g. (0.20 mole) of hexyl chlorocarbonate were added dropwise (15-20 min.). The mixture was then stirred until it warmed to about room temperature (90 min.). The oil which formed was separated from the aqueous phase and dried over anhydrous calcium sulfate. The material was filtered and distilled, but crystalline solid precipitated from the product. The distilled material was filtered to remove the solid and redistilled. Again the crystalline solid precipitated and was removed by washing the product with 7 ml. of 1N nitric acid-0.1N silver nitrate solution. Qualitative tests indicated the solid to be 2-pentylpiperidine hydrochloride. On redistillation the oil yielded 26.5 g. (47%) of 2-pentylpiperidine-1-carboxylic acid, hexyl ester, boiling at 144-148°/1.0 mm.

## 2-Pentylpiperidine-1-carboxylic Acid, Hexyl Ester

Structural Formula:



| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . | $C_{17}H_{33}NO_2$ |
| Molecular Weight . . . . . . . . . . . . | 283.44 |
| Boiling Point . . . . . . . . . . . . . . | 144-148°/1.0 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . . | 1.4590 |
| Yield of Product, % . . . . . . . . . . | 47 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 72.03 | .... | 72.21 |
| Hydrogen, % . | 11.73 | .... | 11.74 |

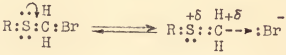
# CHAPTER IV

# PREPARATION OF BROMOMETHYL ETHYL SULFIDE AND REACTION PRODUCTS WITH 2-ALKYL-PIPERIDINES

## Review of Literature

Halomethyl alkyl sulfides have been prepared by a number of workers (15, 20, 23, 25). All the reports used essentially the method reported by Bohme (15). A mixture of ethyl mercaptan and paraformaldehyde was treated with dry hydrogen halide to catalyze the formation of the hemimercaptal of formaldehyde. Continued addition of hydrogen halide resulted in the conversion of the hemimercaptal to the halomethyl ethyl sulfide.

The reaction of halomethyl ethyl sulfide with amines should proceed by the same mechanism as that encountered with normal alkyl halides. The reaction should be somewhat faster due to the increased reactivity of the carbon-halogen bond toward neucleophylic attacking reagents. The increased reactivity is a result of a tendency for the unshared pairs of electrons on the sulfur atom, to shift toward the methylene group, weakening the carbon-bromine bond. This effect may be generalized according to the following illustration:



$$R:\underset{\cdot\cdot}{\overset{\cdot\cdot}{S}}:\underset{H}{\overset{H}{C}}:Br \rightleftharpoons R:\underset{\cdot\cdot}{\overset{+\delta}{S}}::\underset{H}{\overset{H+\delta}{C}} \dashrightarrow :\overset{-}{Br}$$

R represents any alkyl group and R' represents either hydrogen or alkyl groups of ammonia, primary or secondary amines. The partial positive charge on the methylene carbon offers an avenue of attack by the nucleophylic amine.

## Experimental Work

The method for the preparation of bromomethyl ethyl sulfide used in this work is that described by Bohme, et.al. (25).

The general method used in carrying out the reaction of bromomethyl ethyl sulfide with the piperidines was to allow the piperidines and bromomethyl ethyl sulfide to react in the presence of an alkaline material such as potassium carbonate which reacted with the hydrogen bromide liberated in the initial reaction. Except in the case of the reaction with 2-methylpiperidine this was done by means of a two phase reaction mixture incorporating aqueous potassium carbonate or sodium hydroxide and an ether solution of the amine.

Following are detailed directions for the preparation of the bromomethyl ethyl sulfide and its reaction w with each of the 2-alkylpiperidines. After each procedure is a data sheet with the equation for synthesis of the compound and a list of some of the properties of the compound prepared.

All of the 1-ethylthiomethyl-2-alkylpiperidines prepared are new to the literature.

## Bromoethyl Ethyl Sulfide

A mixture of 43 g. of paraformaldehyde and 89 g. (1.43 mole) of ethyl mercaptan was placed in a 500 ml. flask fitted with an ice-water cooled condenser and a gas-delivery tube. Dry hydrogen bromide was bubbled into the solution. After about two minutes, a vigorous reaction started and the flask was cooled in an ice bath. After the reaction had subsided, the cooling bath was removed. When the mixture appeared to be saturated (1-2 hr.), the flow of hydrogen bromide was stopped and 35 g. of calcium chloride was added. After twelve hours dry air was blown through the mixture for two and a half hours. Twenty-five grams of calcium chloride was added and dry air was again passed through the mixture for two and a half hours. The organic layer was separated from the aqueous phase and the aqueous phase was washed with two 75 ml. portions of ether. The combined ether washings were evaporated and the residue was added to the organic layer. On distillation this material yielded 70 g. (32%) of bromomethyl ethyl sulfide boiling at 66-69°/40 mm.

## Bromomethyl Ethyl Sulfide

Equation for Synthesis:

$$C_2H_5\text{-S-H} + H\overset{O}{\overset{\|}{C}}\text{-H} + HBr \longrightarrow C_2H_5\text{-S-}CH_2\text{-Br} + H_2O$$

| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . . | $C_3H_7BrS$ |
| Molecular Weight . . . . . . . . . . . . . . | 155.07 |
| Boiling Point . . . . . . . . . . . . . . . | 66-69°/40 mm. |
| Yield of Product, % . . . . . . . . . . . . | 32 |

Solubility:

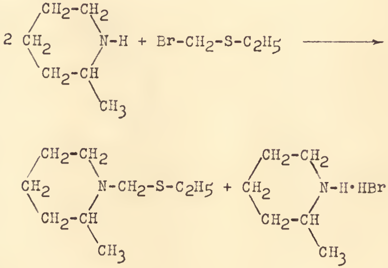
| Insoluble | Soluble |
|---|---|
| Water (decomp.) | Ether |
| | Benzene |

### 1-Ethylthiomethyl-2-methylpiperidine

To a cooled solution of 19.8 g. (0.20 mole) of 2-methylpiperidine in 150 ml. of ether in a 250 ml. Erlenmeyer flask, 15.5 g. (0.10 mole) of bromomethyl ethyl sulfide were added slowly (15-20 min.) with swirling. Thirty minutes after the addition was completed the mixture was filtered to remove the 2-methylpiperidine hydrobromide formed and the ether solution was dried over anhydrous potassium carbonate. The solution was decanted and low-boiling material was removed by means of water-pump vacuum and a steam bath. On distillation, the remaining oil yielded 11.6 g. (67%) of 1-ethylthiomethyl-2-methylpiperidine, boiling at 62.5°/1.0 mm.

## 1-Ethylthiomethyl-2-methylpiperidine

Equation for Synthesis:



| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . | $C_9H_{19}NS$ |
| Molecular Weight . . . . . . . . . . . . | 173.31 |
| Boiling Point . . . . . . . . . . . . . . | $62.5^\circ$/1.0 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . . | 1.4972 |
| Yield of Product, % . . . . . . . . . . . | 67 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

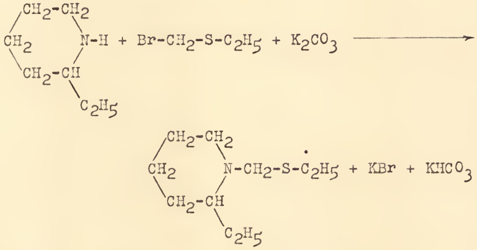
| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 62.37 | .... | 62.54 |
| Hydrogen, % . | 11.05 | .... | 11.12 |

## 1-Ethylthiomethyl-2-ethylpiperidine

A mixture of 100 g. of ice, 100 ml. of water and 8.0 g. of potassium carbonate was placed in an 800 ml. beaker and stirred with a magnetic stirrer until the potassium carbonate was dissolved. Stirring was reduced to a moderate rate and a solution of 4.5 g. (0.04 mole) of 2-ethylpiperidine in 100 ml. of ether was introduced. With continued moderate stirring a solution of 9.0 g. (0.058 mole) of bromomethyl ethyl sulfide in 50 ml. of ether was added dropwise (75 min.). The mixture was stirred for one hour after the addition was completed. The ether layer was separated from the aqueous phase and dried over anhydrous potassium carbonate. The ether solution was decanted and low-boiling material was removed by means of water-pump vacuum and a steam bath. On distillation, the remaining oil yielded 5.5 g. (74%) of 1-ethylthiomethyl-2-ethylpiperidine, boiling at 80°/1.0 mm.

## 1-Ethylthiomethyl-2-ethylpiperidine

Equation for Synthesis:



| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . . | $C_{10}H_{21}NS$ |
| Molecular Weight . . . . . . . . . . . . . | 187.33 |
| Boiling Point . . . . . . . . . . . . . . . | 80°/1.0 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . . . | 1.5003 |
| Yield of Product, % . . . . . . . . . . . | 74 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

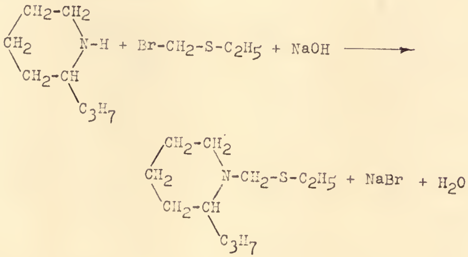
| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 64.12 | .... | 64.19 |
| Hydrogen, % . | 11.30 | .... | 11.40 |

### 1-Ethylthiomethyl-2-propylpiperidine

To a cooled solution of 12.7 g. (0.1 mole) of 2-propylpiperidine in 150 ml. of ether in an Erlenmeyer flask, 15.5 g. (0.10 mole) of bromomethyl ethyl sulfide were added. With continued cooling and occasional swirling, a solution of 4 g. (0.10 mole) of sodium hydroxide in 20 ml. of water was added in units of 10 ml., 5 ml., 2.5 ml., 1.3 ml. and 1.2 ml. at intervals of twenty to thirty minutes. After the addition of sodium hydroxide solution was completed, 50 ml. of water were added and the mixture was shaken frequently for five hours. The ether solution was separated from the aqueous phase and dried over anhydrous potassium carbonate. The solution was decanted and low-boiling material was removed by means of water-pump vacuum and a steam bath. On distillation, the remaining oil yielded 11.6 g. (57.7%) of 1-ethylthiomethy-2-propylpiperidine, boiling at 88°/1.0 mm.

## 1-Ethylthiomethyl-2-propylpiperidine

Equation for Synthesis:



| | |
|---|---|
| Molecular Formula | $C_{11}H_{23}NS$ |
| Molecular Weight | 201.36 |
| Boiling Point | 88°/1.0 mm. |
| $N_D^{25}$ | 1.4945 |
| Yield of Product, % | 57.7 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

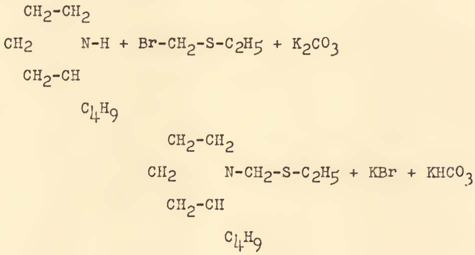
| | Calculated | Found |
|---|---|---|
| Carbon, % | 65.61 | 65.33 |
| Hydrogen, % | 11.51 | 11.89 |

### 1-Ethylthiomethyl-2-butylpiperidine

A mixture of 100 g. of ice and 15 g. of potassium carbonate was placed in an 800 ml. beaker and stirred with a magnetic stirrer until the potassium carbonate was dissolved. Stirring was reduced to a moderate rate, and a solution of 14.1 g. (0.10 mole) of 2-butylpiperidine in 100 ml. of ether was introduced. With continued slow stirring, a solution of 15.5 g. (0.10 mole) of bromomethyl ethyl sulfide in 50 ml. of ether was added dropwise (30 min.). The mixture was stirred for one hour after the addition was completed. The ether layer was separated from the aqueous phase and dried over anhydrous potassium carbonate. The ether solution was decanted and low-boiling material was removed by means of water-pump vacuum and a steam bath. On distillation, the remaining oil yielded 15.5 g. (72%) of 1-ethylthiomethyl-2-butylpiperidine, boiling at 97.5-99°/1.0 mm.

## 1-Ethylthiomethyl-2-butylpiperidine

Equation for Synthesis:


CH2-CH2
CH2 N-H + Br-CH2-S-C2H5 + K2CO3
CH2-CH
C4H9
CH2-CH2
CH2 N-CH2-S-C2H5 + KBr + KHCO3
CH2-CH
C4H9

| | |
|---|---|
| Molecular Formula . . . . . . . . . . . | $C_{12}H_{25}NS$ |
| Molecular Weight . . . . . . . . . . . | 215.39 |
| Boiling Point . . . . . . . . . . . . . | 97.5-99°/1.0 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . | 1.4916 |
| Yield of Product, % . . . . . . . . . . | 72 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

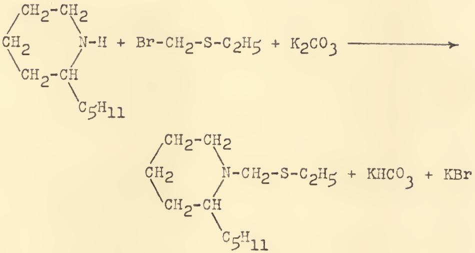
| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 66.91 | .... | 66.54 |
| Hydrogen, % . | 11.70 | .... | 11.48 |

### 1-Ethylthiomethyl-2-pentylpiperidine

A mixture of 100 g. of ice and 15 g. of potassium carbonate was placed in an 800 ml. beaker and stirred with a magnetic stirrer until the potassium carbonate was dissolved. Stirring was reduced to a moderate rate, and a solution of 15.5 g. (0.10 mole) of 2-pentylpiperidine in 100 ml. of ether was introduced. With continued moderate stirring, a solution of 15.5 g. (0.10 mole) of bromomethyl ethyl sulfide in 50 ml. of ether was added dropwise (20 min.). The mixture was stirred for two hours after the addition was completed. The ether layer was separated from the aqueous phase and dried over anhydrous potassium carbonate. The ether solution was decanted and low-boiling material was removed by means of water-pump vacuum and a steam bath. On distillation the remaining oil yielded 13 g. (56.5%) of 1-ethylthiomethyl-2-pentylpiperidine boiling at 104-108°/1.0 mm.

## 1-Ethylthiomethyl-2-pentylpiperidine

Equation for Synthesis:



| | |
|---|---|
| Molecular Formula . . . . . . . . . . . . | $C_{13}H_{27}NS$ |
| Molecular Weight . . . . . . . . . . . . | 229.42 |
| Boiling Point . . . . . . . . . . . . . . | 104-108°/1.0 mm. |
| $N_D^{25}$ . . . . . . . . . . . . . . . . . . . . . | 1.4856 |
| Yield of Product, % . . . . . . . . . . . | 56.5 |

Solubility:

| Insoluble | Soluble |
|---|---|
| Water | Ether |
| | Alcohol |
| | Benzene |

Analyses:

| | Calculated | | Found |
|---|---|---|---|
| Carbon, % ... | 68.05 | .... | 67.91 |
| Hydrogen, % . | 11.86 | .... | 11.51 |

## SUMMARY

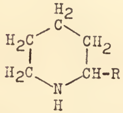
2-Alkylpiperidines, in which the alkyl group varies from methyl through pentyl were prepared. The homologs higher than methyl were prepared by a general method. All the 2-alkylpiperidines prepared except 2-butylpiperidine have been prepared by methods similar to that in this work. 2-Butylpiperidine has also been previously reported, but by a different method. A series of seven carbamic acid esters of each piperidine was prepared. All of these carbamic acid esters except 2-propylpiperidine-1-carboxylic acid, ethyl ester, are new to the literature.

1-Ethylthiomethyl derivatives were also prepared from each of the 2-alkylpiperidines. All of the 1-ethylthiomethyl derivatives are new to the literature.

The properties which were determined of the compounds prepared in this work are summarized in the following tables.

## TABLE I

### 2-R Piperidine

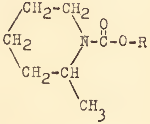


| R | Molecular Formula | Molecular Weight | Boiling Point, °C | $N_D^{25}$ | Yield |
|---|---|---|---|---|---|
| Methyl | $C_6H_{13}N$ | 99.17 | 117-118.5<br>atmospheric | 1.4463 | 99.0 |
| Ethyl | $C_7H_{15}N$ | 113.20 | 141-141<br>atmospheric | 1.4494 | 46.0 |
| Propyl | $C_8H_{17}N$ | 127.23 | 167-168<br>atmospheric | 1.4490 | 46.6 |
| Butyl | $C_9H_{19}N$ | 141.25 | 98.8-99<br>@ 40 mm. | 1.4508 | 41.5 |
| Pentyl | $C_{10}H_{21}N$ | 155.28 | 115.5-117<br>@ 40 mm. | 1.4526 | 63.5 |

## TABLE II

## 2-Methylpiperidine-1-carboxylic Acid

## R Ester

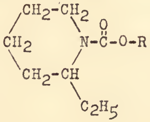


| R | Molecular Formula | Molecular Weight | Boiling Point °C/1.0 mm. | $N_D^{25}$ | Yield |
|---|---|---|---|---|---|
| Methyl | $C_8H_{15}O_2N$ | 157.21 | 54-58 | 1.4604 | 51.3 |
| Ethyl | $C_9H_{17}O_2N$ | 171.24 | 60 | 1.4558 | 60.0 |
| Propyl | $C_{10}H_{19}O_2N$ | 185.26 | 69-70 | 1.4559 | 54.5 |
| Butyl | $C_{11}H_{21}O_2N$ | 199.29 | 80-82 | 1.4563 | 76.0 |
| 2-Methyl-propyl | $C_{11}H_{21}O_2N$ | 199.29 | 76 | 1.4539 | 82.0 |
| Pentyl | $C_{12}H_{23}O_2N$ | 213.31 | 92 | 1.4571 | 71.0 |
| Hexyl | $C_{13}H_{25}O_2N$ | 227.34 | 103 | 1.4579 | 68.0 |

## TABLE III

## 2-Ethylpiperidine-1-carboxylic Acid

## R Ester

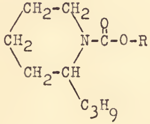


| R | Molecular Formula | Molecular Weight | Boiling Point °C/1.0 mm. | $N_D^{25}$ | Yield |
|---|---|---|---|---|---|
| Methyl | $C_9H_{17}O_2N$ | 171.24 | 62-64 | 1.4960 | 57.0 |
| Ethyl | $C_{10}H_{19}O_2N$ | 185.26 | 68.5-70 | 1.4560 | 64.2 |
| Propyl | $C_{11}H_{21}O_2N$ | 199.29 | 80-81 | 1.4559 | 71.8 |
| Butyl | $C_{12}H_{23}O_2N$ | 213.31 | 91.5-92 | 1.4567 | 78.9 |
| 2-Methyl-propyl | $C_{12}H_{23}O_2N$ | 213.31 | 87.89 | 1.4538 | 87.4 |
| Pentyl | $C_{13}H_{25}O_2N$ | 227.34 | 104-106 | 1.4570 | 72.0 |
| Hexyl | $C_{14}H_{27}O_2N$ | 241.37 | 115.5-117.5 | 1.4546 | 70.3 |

## TABLE IV

## 2-Propylpiperidine-1-carboxylic Acid

## R Ester

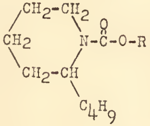


| R | Molecular Formula | Molecular Weight | Boiling Point °C/1.0 mm. | $N_D^{25}$ | Yield |
|---|---|---|---|---|---|
| Methyl | $C_{10}H_{19}O_2N$ | 185.25 | 68 | 1.4604 | 73.0 |
| Ethyl | $C_{11}H_{21}O_2N$ | 199.29 | 65-67 @ 0.7 mm. | 1.4570 | 40.5 |
| Propyl | $C_{12}H_{23}O_2N$ | 213.31 | 89 | 1.4570 | 87.0 |
| Butyl | $C_{13}H_{25}O_2N$ | 227.34 | 90.5-91.5 | 1.4549 | 74.0 |
| 2-Methyl-propyl | $C_{13}H_{25}O_2N$ | 227.34 | 93.5-94 | 1.4560 | 61.0 |
| Pentyl | $C_{14}H_{27}O_2N$ | 241.37 | 105-107 | 1.4578 | 71.0 |
| Hexyl | $C_{15}H_{29}O_2N$ | 255.39 | 119-120 | 1.4583 | 74.0 |

## TABLE V

## Butylpiperidine-1-carboxylic Acid

## R Ester

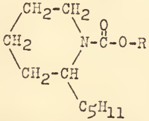


| R | Molecular Formula | Molecular Weight | Boiling Point °C/1.0 mm. | $N_D^{25}$ | Yield |
|---|---|---|---|---|---|
| Methyl | $C_{11}H_{21}O_2N$ | 199.29 | 84-86 | 1.4610 | 65.0 |
| Ethyl | $C_{12}H_{23}O_2N$ | 213.31 | 90.5-92 | 1.4573 | 71.0 |
| Propyl | $C_{13}H_{25}O_2N$ | 227.34 | 100 | 1.4588 | 39.0 |
| Butyl | $C_{14}H_{27}O_2N$ | 241.37 | 110.5 | 1.4580 | 66.0 |
| 2-Methyl-propyl | $C_{14}H_{27}O_2N$ | 241.37 | 108-109 | 1.4561 | 78.0 |
| Pentyl | $C_{15}H_{29}O_2N$ | 255.39 | 121-122 | 1.4581 | 81.0 |
| Hexyl | $C_{16}H_{31}O_2N$ | 269.42 | 134-135 | 1.4578 | 59.5 |

# TABLE VI

## 2-Pentylpiperidine-1-carboxylic Acid

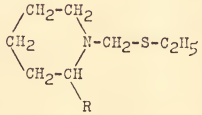
## R Ester



| R | Molecular Formula | Molecular Weight | Boiling Point °C/1.0 mm. | $N_D^{25}$ | Yield |
|---|---|---|---|---|---|
| Methyl | $C_{12}H_{23}O_2N$ | 213.31 | 91.5 | 1.4609 | 59.0 |
| Ethyl | $C_{13}H_{25}O_2N$ | 227.34 | 100-103 | 1.4579 | 78.0 |
| Propyl | $C_{14}H_{27}O_2N$ | 241.37 | 112-113 | 1.4580 | 76.0 |
| Butyl | $C_{15}H_{29}O_2N$ | 255.39 | 122-124 | 1.4586 | 75.0 |
| 2-Methyl-propyl | $C_{15}H_{29}O_2N$ | 255.39 | 120-122 | 1.4564 | 76.0 |
| Pentyl | $C_{16}H_{31}O_2N$ | 269.42 | 134 | 1.4587 | 23.0 |
| Hexyl | $C_{17}H_{33}O_2N$ | 283.44 | 144-148 | 1.4590 | 47.0 |

## TABLE VII

## 1-Ethylthiomethyl-2-R Piperidine



| R | Molecular Formula | Molecular Weight | Boiling Point, °C | $N_D^{25}$ | Yield |
|---|---|---|---|---|---|
| Methyl | $C_9H_{19}NS$ | 173.31 | 62.5 | 1.4972 | 67.0 |
| Ethyl | $C_{10}H_{21}NS$ | 187.33 | 80.0 | 1.5003 | 74.0 |
| Propyl | $C_{11}H_{23}NS$ | 201.36 | 88.0 | 1.4945 | 57.7 |
| Butyl | $C_{12}H_{25}NS$ | 215.39 | 97.5-99 | 1.4916 | 72.0 |
| Pentyl | $C_{13}H_{27}NS$ | 229.42 | 104-108 | 1.4856 | 56.5 |

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# BIOGRAPHICAL ITEMS

Bernard A. Parkin, Jr. was born October 18, 1926 in Jacksonville, Florida. After serving in the Army for twenty-seven months, he entered the University of Florida in February, 1947. After receiving the degree of Bachelor of Arts in Chemistry in July, 1950, he entered graduate school at the University of Florida in September of that same year. During the course of his studies toward the Doctor of Philosophy degree, he first held a Graduate Assistantship and then a Teaching Assistantship in the Department of Chemistry. He is a member of Phi Eta Sigma, freshman honorary fraternity and Gamma Sigma Epsilon, honorary chemical fraternity.

COMMITTEE REPORT

This dissertation was prepared under the direction of the Chairman of the candidate's Supervisory Committee. It was submitted to the Graduate Council and was approved as partial fulfillment of the requirements for the degree of Doctor of Philosophy.

Date ____________________

C. F. Byers

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